

## SEQUENCE LISTING

<110> Bayer Pharmaceuticals Corporation  
Clairmont, Kevin  
Lumb, Kevin  
Buckholz, Thomas  
Salhanick, Arthur

<120> PITUITARY ADENYLATE CYCLASE ACTIVATING PEPTIDE (PACAP) RECEPTOR  
(VPAC2) AGONISTS AND THEIR PHARMACOLOGICAL METHODS OF USE

<130> 5189

<150> US 60/539,550  
<151> 2004-01-27

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<151> 2004-04-29

<160> 155

<170> PatentIn version 3.3

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<400> 63

His Ser Asp Ala Val Phe Thr Asp Asn Tyr Thr Arg Leu Arg Lys Gln  
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Met Ala Ala Lys Lys Tyr Leu Gln Ser Ile Lys Gln Lys Pro  
20 25 30

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<400> 64

His Ser Asp Ala Val Phe Thr Asp Asn Tyr Thr Arg Leu Arg Lys Gln  
1 5 10 15

Met Ala Ala Lys Lys Tyr Leu Gln Ser Ile Lys Gln Lys Gln  
20 25 30

<210> 65  
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<400> 65

His Ser Asp Ala Val Phe Thr Asp Asn Tyr Thr Arg Leu Arg Lys Gln  
1 5 10 15

Met Ala Ala Lys Lys Tyr Leu Gln Ser Ile Lys Gln Lys Ser  
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<400> 66

His Ser Asp Ala Val Phe Thr Asp Asn Tyr Thr Arg Leu Arg Lys Gln  
1 5 10 15

Met Ala Ala Lys Lys Tyr Leu Gln Ser Ile Lys Gln Lys Thr  
20 25 30

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<400> 67

His Ser Asp Ala Val Phe Thr Asp Asn Tyr Thr Arg Leu Arg Lys Gln  
1 5 10 15

Met Ala Ala Lys Lys Tyr Leu Gln Ser Ile Lys Gln Lys Val  
20 25 30

<210> 68  
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<400> 68

His Ser Asp Ala Val Phe Thr Asp Asn Tyr Thr Arg Leu Arg Lys Gln  
1 5 10 15

Met Ala Ala Lys Lys Tyr Leu Gln Ser Ile Lys Gln Lys Trp  
20 25 30

<210> 69  
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<400> 69

His Ser Asp Ala Val Phe Thr Asp Asn Tyr Thr Arg Leu Arg Lys Gln  
1 5 10 15

Met Ala Ala Lys Lys Tyr Leu Gln Ser Ile Lys Gln Lys Tyr  
20 25 30

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<400> 70

His Ser Asp Ala Val Phe Thr Asp Asn Tyr Thr Arg Leu Arg Lys Gln  
1 5 10 15

Met Ala Gly Lys Lys Tyr Leu Gln Ser Ile Lys Gln Arg Ile  
20 25 30

<210> 71  
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His Ser Asp Ala Val Phe Thr Asp Asn Tyr Thr Arg Leu Arg Lys Gln  
1 5 10 15

Met Ala Lys Lys Lys Tyr Leu Gln Ser Ile Lys Gln Arg Ile  
20 25 30

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<400> 72

His Ser Asp Ala Val Phe Thr Asp Asn Tyr Thr Arg Leu Arg Lys Gln  
1 5 10 15

Met Ala Ser Lys Lys Tyr Leu Gln Ser Ile Lys Gln Arg Ile  
20 25 30

<210> 73  
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<400> 73

His Ser Asp Ala Val Phe Thr Asp Asn Tyr Thr Arg Leu Arg Lys Gln  
1 5 10 15

Met Ala Ala Lys Lys Tyr Leu Gln Ser Ile Pro Gln Arg Ile  
20 25 30

<210> 74  
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<400> 74

His Ser Asp Ala Val Phe Thr Asp Asn Tyr Thr Arg Leu Arg Lys Gln  
1 5 10 15

Met Ala Ser Lys Lys Tyr Leu Gln Ser Ile Arg Gln Arg Ile  
20 25 30

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<400> 75

His Ser Asp Ala Val Phe Thr Asp Gln Tyr Thr Arg Leu Arg Lys Gln  
1 5 10 15

Val Ala Ala Lys Lys Tyr Leu Gln Ser Ile Lys Asn Lys Arg Tyr  
20 25 30

<210> 76

<211> 31

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<213> Homo sapiens

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<223> ACETYLATION

<400> 76

His Ser Asp Ala Val Phe Thr Asp Gln Tyr Thr Arg Leu Arg Lys Gln  
1 5 10 15

Met Ala Ala Lys Lys Tyr Leu Gln Ser Ile Lys Asn Lys Arg Tyr  
20 25 30

<210> 77

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<223> ACETYLATION

<400> 77

His Ser Asp Ala Val Phe Thr Asp Gln Tyr Thr Arg Leu Arg Lys Gln  
1 5 10 15

Val Ala Ala Lys Lys Tyr Leu Gln Ser Ile Lys Asn Lys  
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<210> 78

<211> 31

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<400> 78

His Thr Glu Ala Val Phe Thr Asp Gln Tyr Thr Arg Leu Arg Lys Gln  
1 5 10 15

Val Ala Ala Lys Lys Tyr Leu Gln Ser Ile Lys Asn Lys Arg Tyr  
20 25 30

<210> 79  
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<400> 79

His Ser Asp Ala Val Phe Thr Asp Gln Tyr Thr Arg Leu Arg Lys Gln  
1 5 10 15

Leu Ala Val Lys Lys Tyr Leu Gln Asp Ile Lys Asn Gly Gly Thr  
20 25 30

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<400> 80

His Ser Asp Ala Val Phe Thr Asp Gln Tyr Thr Arg Leu Arg Lys Gln  
1 5 10 15

Met Ala Ala Lys Lys Tyr Leu Gln Ser Ile Lys Asn Lys Arg  
20 25 30

<210> 81  
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<400> 81

His Ser Asp Ala Val Phe Thr Asp Gln Tyr Thr Arg Leu Arg Lys Gln  
1 5 10 15

Leu Ala Ala Lys Lys Tyr Leu Gln Thr Ile Lys Asn Lys Arg Tyr  
20 25 30

<210> 82

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<400> 82

His Ser Asp Ala Val Phe Thr Asp Gln Tyr Thr Arg Leu Arg Lys Gln  
1 5 10 15

Met Ala Ala Lys Lys Tyr Leu Gln Thr Ile Lys Asn Lys Arg Tyr  
20 25 30

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<400> 83

His Ser Asp Ala Val Phe Thr Asp Gln Tyr Thr Arg Leu Arg Lys Gln  
1 5 10 15

Met Ala Ala His Lys Tyr Leu Gln Ser Ile Lys Asn Lys Arg Tyr  
20 25 30

<210> 84  
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<400> 84

His Ser Asp Ala Val Phe Thr Asp Gln Tyr Thr Arg Leu Arg Lys Gln  
1 5 10 15

Met Ala Ala Lys His Tyr Leu Gln Ser Ile Lys Asn Lys Arg Tyr  
20 25 30

<210> 85  
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<400> 85

His Ser Asp Ala Val Phe Thr Asp Gln Tyr Thr Arg Leu Arg Lys Gln  
1 5 10 15

Met Ala Gly Lys Lys Tyr Leu Gln Ser Ile Lys Asn Lys Arg  
20 25 30

<210> 86  
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<400> 86

His Ser Asp Ala Val Phe Thr Asp Gln Tyr Thr Arg Leu Arg Lys Gln  
1 5 10 15

Met Ala Lys Lys Lys Tyr Leu Gln Ser Ile Lys Asn Lys Arg  
20 25 30

<210> 87  
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<400> 87

His Ser Asp Ala Val Phe Thr Asp Gln Tyr Thr Arg Leu Arg Lys Gln  
1 5 10 15

Met Ala Arg Lys Lys Tyr Leu Gln Ser Ile Lys Asn Lys Arg  
20 25 30

<210> 88  
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<400> 88

His Ser Asp Ala Val Phe Thr Asp Gln Tyr Thr Arg Leu Arg Lys Gln  
1 5 10 15

Met Ala Ser Lys Lys Tyr Leu Gln Ser Ile Lys Asn Lys Arg  
20 25 30

<210> 89  
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<222> (1)..(30)  
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<400> 89

His Ser Asp Ala Val Phe Thr Asp Gln Tyr Thr Arg Leu Arg Lys Gln  
1 5 10 15

Met Ala Ala Lys Lys Tyr Leu Gln Ser Ile Pro Asn Lys Arg  
20 25 30

<210> 90  
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<400> 90

His Ser Asp Ala Val Phe Thr Asp Gln Tyr Thr Arg Leu Arg Lys Gln  
1 5 10 15

Met Ala Ala Lys Lys Tyr Leu Gln Ser Ile Gln Asn Lys Arg  
20 25 30

<210> 91  
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<400> 91

His Ser Asp Ala Val Phe Thr Asp Gln Tyr Thr Arg Leu Arg Lys Gln  
1 5 10 15

Met Ala Ala Lys Lys Tyr Leu Gln Ser Ile Arg Asn Lys Arg  
20 25 30

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His Ser Asp Ala Val Phe Thr Asp Gln Tyr Thr Arg Leu Arg Lys Gln  
1 5 10 15

Met Ala Ala Lys Lys Tyr Leu Gln Ser Ile Lys Asn Arg Arg  
20 25 30

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<400> 93

His Ser Asp Ala Val Phe Thr Asp Gln Tyr Thr Arg Leu Arg Lys Gln  
1 5 10 15

Met Ala Ala Lys Lys Tyr Leu Gln Ser Ile Lys Asn Lys Ala  
20 25 30

<210> 94  
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<400> 94

His Ser Asp Ala Val Phe Thr Asp Gln Tyr Thr Arg Leu Arg Lys Gln  
1 5 10 15

Met Ala Ala Lys Lys Tyr Leu Gln Ser Ile Lys Asn Lys Phe  
20 25 30

<210> 95  
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<400> 95

His Ser Asp Ala Val Phe Thr Asp Gln Tyr Thr Arg Leu Arg Lys Gln  
1 5 10 15

Met Ala Ala Lys Lys Tyr Leu Gln Ser Ile Lys Asn Lys His  
20 25 30

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<400> 96

His Ser Asp Ala Val Phe Thr Asp Gln Tyr Thr Arg Leu Arg Lys Gln  
1 5 10 15

Met Ala Ala Lys Lys Tyr Leu Gln Ser Ile Lys Asn Lys Ile  
20 25 30

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His Ser Asp Ala Val Phe Thr Asp Gln Tyr Thr Arg Leu Arg Lys Gln  
1 5 10 15

Met Ala Ala Lys Lys Tyr Leu Gln Ser Ile Lys Asn Lys Lys  
20 25 30

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<400> 98

His Ser Asp Ala Val Phe Thr Asp Gln Tyr Thr Arg Leu Arg Lys Gln  
1 5 10 15

Met Ala Ala Lys Lys Tyr Leu Gln Ser Ile Lys Asn Lys Leu  
20 25 30

<210> 99

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<223> ACETYLATION

<400> 99

His Ser Asp Ala Val Phe Thr Asp Gln Tyr Thr Arg Leu Arg Lys Gln  
1 5 10 15

Met Ala Ala Lys Lys Tyr Leu Gln Ser Ile Lys Asn Lys Met  
20 25 30

<210> 100

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<223> ACETYLATION

<400> 100

His Ser Asp Ala Val Phe Thr Asp Gln Tyr Thr Arg Leu Arg Lys Gln  
1 5 10 15

Met Ala Ala Lys Lys Tyr Leu Gln Ser Ile Lys Asn Lys Pro  
20 25 30

<210> 101

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<400> 101

His Ser Asp Ala Val Phe Thr Asp Gln Tyr Thr Arg Leu Arg Lys Gln  
1 5 10 15

Met Ala Ala Lys Lys Tyr Leu Gln Ser Ile Lys Asn Lys Gln  
20 25 30

<210> 102  
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<212> PRT  
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<400> 102

His Ser Asp Ala Val Phe Thr Asp Gln Tyr Thr Arg Leu Arg Lys Gln  
1 5 10 15

Met Ala Ala Lys Lys Tyr Leu Gln Ser Ile Lys Asn Lys Ser  
20 25 30

<210> 103  
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<400> 103

His Ser Asp Ala Val Phe Thr Asp Gln Tyr Thr Arg Leu Arg Lys Gln  
1 5 10 15

Met Ala Ala Lys Lys Tyr Leu Gln Ser Ile Lys Asn Lys Thr  
20 25 30

<210> 104  
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<400> 104

His Ser Asp Ala Val Phe Thr Asp Gln Tyr Thr Arg Leu Arg Lys Gln  
1 5 10 15

Met Ala Ala Lys Lys Tyr Leu Gln Ser Ile Lys Asn Lys Val  
20 25 30

<210> 105

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<400> 105

His Ser Asp Ala Val Phe Thr Asp Gln Tyr Thr Arg Leu Arg Lys Gln  
1 5 10 15

Met Ala Ala Lys Lys Tyr Leu Gln Ser Ile Lys Asn Lys Trp  
20 25 30

<210> 106  
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<212> PRT  
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<222> (1)..(30)  
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<400> 106

His Ser Asp Ala Val Phe Thr Asp Gln Tyr Thr Arg Leu Arg Lys Gln  
1 5 10 15

Met Ala Ala Lys Lys Tyr Leu Gln Ser Ile Lys Asn Lys Tyr  
20 25 30

<210> 107  
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<212> PRT  
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<222> (1)..(30)  
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<400> 107

His Ser Asp Ala Val Phe Thr Asp Gln Tyr Thr Arg Leu Arg Lys Gln  
1 5 10 15

Met Ala Gly Lys Lys Tyr Leu Gln Ser Ile Lys Asn Arg Ile  
20 25 30

<210> 108  
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<400> 108

His Ser Asp Ala Val Phe Thr Asp Gln Tyr Thr Arg Leu Arg Lys Gln  
1 5 10 15

Met Ala Lys Lys Lys Tyr Leu Gln Ser Ile Lys Asn Arg Ile  
20 25 30

<210> 109  
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<400> 109

His Ser Asp Ala Val Phe Thr Asp Gln Tyr Thr Arg Leu Arg Lys Gln  
1 5 10 15

Met Ala Ser Lys Lys Tyr Leu Gln Ser Ile Lys Asn Arg Ile  
20 25 30

<210> 110  
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<212> PRT  
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<400> 110

His Ser Asp Ala Val Phe Thr Asp Gln Tyr Thr Arg Leu Arg Lys Gln  
1 5 10 15

Met Ala Ala Lys Lys Tyr Leu Gln Ser Ile Pro Asn Arg Ile  
20 25 30

<210> 111  
<211> 30  
<212> PRT  
<213> Homo sapiens

<220>  
<221> MOD\_RES  
<222> (1)..(30)  
<223> ACETYLATION

<400> 111

His Ser Asp Ala Val Phe Thr Asp Gln Tyr Thr Arg Leu Arg Lys Gln  
1 5 10 15

Met Ala Ser Lys Lys Tyr Leu Gln Ser Ile Arg Asn Arg Ile  
20 25 30

<210> 112  
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<212> PRT  
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<220>  
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<220>  
<221> MOD\_RES  
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<223> ACETYLATION

<400> 112

His Ser Asp Ala Val Phe Thr Asp Gln Tyr Thr Arg Leu Arg Lys Gln  
1 5 10 15

Val Ala Ala Lys Lys Tyr Leu Gln Ser Ile Lys Gln Lys Arg Tyr Cys  
20 25 30

<210> 113  
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<212> PRT  
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<220>  
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<220>  
<221> MOD\_RES  
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<223> ACETYLATION

<400> 113

His Ser Asp Ala Val Phe Thr Asp Gln Tyr Thr Arg Leu Arg Lys Gln  
1 5 10 15

Met Ala Ala Lys Lys Tyr Leu Gln Ser Ile Lys Gln Lys Arg Tyr Cys  
20 25 30

<210> 114  
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<223> Cysteine at position 30 is PEGylated.

<220>  
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<400> 114

His Ser Asp Ala Val Phe Thr Asp Gln Tyr Thr Arg Leu Arg Lys Gln  
1 5 10 15

Val Ala Ala Lys Lys Tyr Leu Gln Ser Ile Lys Gln Lys Cys  
20 25 30

<210> 115  
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<400> 115

His Thr Glu Ala Val Phe Thr Asp Gln Tyr Thr Arg Leu Arg Lys Gln  
1 5 10 15

Val Ala Ala Lys Lys Tyr Leu Gln Ser Ile Lys Gln Lys Arg Tyr Cys  
20 25 30

<210> 116  
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<220>  
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<400> 116

His Ser Asp Ala Val Phe Thr Asp Gln Tyr Thr Arg Leu Arg Lys Gln  
1 5 10 15

Leu Ala Val Lys Lys Tyr Leu Gln Asp Ile Lys Gln Gly Gly Thr Cys  
20 25 30

<210> 117  
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<223> Cysteine at position 31 is PEGylated.

<220>  
<221> MOD\_RES  
<222> (1)..(31)  
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<400> 117

His Ser Asp Ala Val Phe Thr Asp Gln Tyr Thr Arg Leu Arg Lys Gln  
1 5 10 15

Met Ala Ala Lys Lys Tyr Leu Gln Ser Ile Lys Gln Lys Arg Cys  
20 25 30

<210> 118  
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<220>  
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<223> ACETYLATION

<400> 118

His Ser Asp Ala Val Phe Thr Asp Gln Tyr Thr Arg Leu Arg Lys Gln  
1 5 10 15

Leu Ala Ala Lys Lys Tyr Leu Gln Thr Ile Lys Gln Lys Arg Tyr Cys  
20 25 30

<210> 119  
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<400> 119

His Ser Asp Ala Val Phe Thr Asp Gln Tyr Thr Arg Leu Arg Lys Gln  
1 5 10 15

Met Ala Ala Lys Lys Tyr Leu Gln Thr Ile Lys Gln Lys Arg Tyr Cys  
20 25 30

<210> 120  
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<400> 120

His Ser Asp Ala Val Phe Thr Asp Gln Tyr Thr Arg Leu Arg Lys Gln  
1 5 10 15

Met Ala Ala His Lys Tyr Leu Gln Ser Ile Lys Gln Lys Arg Tyr Cys  
20 25 30

<210> 121  
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<400> 121

His Ser Asp Ala Val Phe Thr Asp Gln Tyr Thr Arg Leu Arg Lys Gln  
1 5 10 15

Met Ala Ala Lys His Tyr Leu Gln Ser Ile Lys Gln Lys Arg Tyr Cys  
20 25 30

<210> 122  
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<400> 122

His Ser Asp Ala Val Phe Thr Asp Gln Tyr Thr Arg Leu Arg Lys Gln  
1 5 10 15

Met Ala Gly Lys Lys Tyr Leu Gln Ser Ile Lys Gln Lys Arg Cys  
20 25 30

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